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CLAIMS

1. A peptide conjugate of the formula I



wherein:

n is from 1 to 10;

X is

- (a) C=O, when the R-X group is attached to:

- (i) the N-terminus of the peptide, or
- (ii) a side chain of the peptide where the functional group of the side chain to which the R-X group is attached is NH_2 or OH; or

- (b) O or NH, when the R-X group is attached to

- (i) the C-terminus of the peptide, or
- (ii) a side chain of the peptide where the functional group of the side chain to which the R-X group is attached is COOH or CONH_2 ; and

R is selected from the group consisting of C_{2-18} alkyl; C_{2-18} alkoxy; C_{2-14} alkenyl containing one or two double bonds; cyclobutyl; cyclopentyl; cyclohexyl optionally monosubstituted with a C_{1-5} straight or branched chain alkyl group; phenyl optionally monosubstituted with a C_{1-5} straight or branched chain alkyl group; and benzyl.

2. A peptide conjugate according to claim 1 wherein n is 1, 2 or 3.

3. A peptide conjugate according to claim 1 wherein ¹¹m is

3 to 20.
4 to 10.

4. A peptide conjugate according to claim 1 wherein R is

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A1

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C₃₋₁₈ alkyl.

5. A peptide conjugate according to claim 4 wherein R is C₃₋₆ branched chain alkyl.

6. A peptide conjugate according to claim 1 wherein R is C₂₋₁₄ alkylenyl containing one double bond.

7. A peptide conjugate according to claim 1 wherein R is C₄₋₈ alkylenyl containing two double bonds.

8. A peptide conjugate according to claim 1 wherein the peptide contains at least one D-amino acid.

9. A peptide conjugate according to claim 1 wherein the peptide is a modulator of apoptosis.

10. A peptide conjugate according to claim 9 wherein the peptide is an inhibitor of apoptosis.

11. A peptide conjugate according to claim 9 wherein the peptide is an inducer of apoptosis.

12. A peptide conjugate according to claim 1 wherein the peptide is an inhibitor of the function of an intracellular biological target.

13. A peptide conjugate according to claim 12 wherein the peptide is an inhibitor of the function of Bcl-2.

14. A peptide conjugate according to claim 13 wherein the peptide binds to the Bcl-2 protein.

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15. A peptide conjugate according to claim 14 wherein the dissociation constant of the peptide for the Bcl-2 protein is no more than about 100 μ M.

16. A peptide conjugate according to claim 15 wherein the dissociation constant of the peptide for the Bcl-2 protein is no more than about 10 μ M.

17. A peptide conjugate according to claim 16 wherein the dissociation constant of the peptide for the Bcl-2 protein is no more than about 1 μ M.

18. A peptide conjugate according to claim 13 wherein the peptide is selected from the group consisting of SEQ ID NO:1 through SEQ ID NO:57, and analogs of such peptides wherein one amino acid is conservatively substituted with another, different amino acid:

19. A peptide conjugate according to claim 18 wherein the peptide is selected from the group consisting of SEQ ID NO:1, SEQ ID NO:30, SEQ ID NO:32, SEQ ID NO:34, SEQ ID NO:55, SEQ ID NO:56 and SEQ ID NO:57.

20. A peptide conjugate according to claim 19 of the formula $\text{CH}_3(\text{CH}_2)_n\text{C(O)}$ -peptide wherein n is from 4 to 16.

21. The peptide conjugate of claim 20 selected from the group consisting of $\text{CH}_3(\text{CH}_2)_{16}\text{COHN}$ -SEQ ID NO:56 and $\text{CH}_3(\text{CH}_2)_8\text{COHN}$ -SEQ ID NO:56.

22. A pharmaceutical composition comprising a pharmaceutical vehicle and a peptide conjugate according to claim 1.

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23. A method for enhancing the cellular uptake of a peptide comprising conjugating said peptide to a carrier moiety $(R-X)_n$, to form a conjugate according to claim 1, wherein R, X and n are defined as in claim 1.

24. A method according to claim 23 wherein the peptide is an inhibitor of the function of an intracellular biological target.

25. A method according to claim 24 wherein the peptide is an inhibitor of the function of Bcl-2.

26. A method for modulating apoptosis in cells of a subject comprising administering to the subject an effective amount of a peptide conjugate according to claim 1 wherein the peptide is a modulator of apoptosis.

27. A method according to claim 26 wherein the peptide is an inhibitor of apoptosis.

28. A method according to claim 26 wherein the peptide is an inducer of apoptosis.

29. A method according to claim 28 wherein the cells induced to undergo apoptosis comprise cancer cells.

30. A method according to claim 28 wherein the cells induced to undergo apoptosis comprise virus-infected cells.

31. A method according to claim 28 wherein the cells induced to undergo apoptosis comprise self-reactive lymphocytes.

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32. A method according to claim 26 wherein the peptide is an inhibitor of Bcl-2 function.

33. A method of reversing Bcl-2-mediated blockage of apoptosis in cancer cells comprising contacting said cells with a peptide conjugate according to claim 13.

34. A method for treating a subject afflicted with a cancer characterized by cancer cells which express Bcl-2 comprising administering to the subject an effective amount of a peptide conjugate according to claim 13.

35. A method according to claim 34 wherein the cancer is selected from the group of cancers consisting of prostate, colorectal, gastric, non-small lung, renal and thyroid cancers, neuroblastoma, melanoma, and acute and chronic lymphocytic and non-lymphocytic leukemia.

36. A method for modulating apoptosis in cells comprising contacting the cells with a conjugate of a molecule which is a modulator of apoptosis and a chemical group of the formula



wherein:

n is from 1 to 10;

X is an atom, chemical bond or chemical group; and

R is selected from the group consisting of C₂₋₁₈ alkyl; C₂₋₁₈ alkoxy; C₂₋₁₄ alkylenyl containing one or two double bonds; cyclobutyl; cyclopentyl; cyclohexyl optionally monosubstituted with a C₁₋₅ straight or branched chain alkyl group; phenyl optionally monosubstituted with a C₁₋₅ straight or branched chain alkyl group; and benzyl.

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37. A method according to claim 36 wherein n is 1, 2 or 3.

38. A method according to claim 36 wherein X is selected from the group consisting of C=O, O and NH.

39. A method according to claim 36 wherein the modulator is an inhibitor of apoptosis.

40. A method according to claim 36 wherein the modulator is an inducer of apoptosis.

41. A method according to claim 40 wherein the cells induced to undergo apoptosis comprise cancer cells, virus-infected cells or self-reactive lymphocytes.

42. A method according to claim 40 wherein the modulator is an inhibitor of Bcl-2 function.

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